CPB FMEA # 22 Failure to prevent hypotension following CPB initiation, Level III.

Friends-

The FMEA this week is the last in a series of three for hypotension during CPB occurring after the management interventions of Level II fail to mitigate the problem. This failure is the rarest but it increases the risk to the patient over Level II. This again comes from material supplied to me by Eric Jenkins, CCT, CCP, FPP and Kevin Griffith, CCP from Ann Arbor. This form of hypotension has often been termed vasoplegia and prompts the use of methylene blue. One article (Fischer 2010) says the frequency is 5-25%. Another author (Gomes 1994) cites a frequency of vasoplegia at 0.8% which I think is more credible.

I really don’t know how to characterize “vasoplegia”. Is it anaphylaxsis and related to a severe immune response? Most patients tolerate CPB well just like most people tolerate consuming lots of peanuts safely. But I have seen a single peanut kill a particular child due to anaphylaxis. However anaphylaxis usually responds to epi, vasoplegia does not; this could be one definition of vasoplegia. Circulatory collapse in septic patients looks like vasoplegia and responds to methylene blue when epi does not work. However vasodilation in sepsis is due to bacterial toxins. Could it be that plasticizers used in CPB circuits cause this problem in only a very few patients who are sensitive to it? Maybe, but that is not something we can currently do anything about in the clinical setting. I have sometimes wondered if we should prime a pump with crystalloid and then rinse the fluid out in an effort to remove some unknown detrimental factor. Sounds like a good student project, to see if patients on a rinsed circuit have less hypotension in general and vasoplegia specifically.

Plasticizers have been researched before without any solid conclusions that I know of. (“Although the overall benefits of medical procedures using PVC devices outweigh the risks associated with exposure to DEHP, more research is needed to determine whether infants and children who undergo intensive therapeutic interventions using DEHP-containing devices are at higher risk for altered health outcomes than infants and children who undergo similar treatments but are not potentially exposed to DEHP.” Calafat et al 2004)

Maybe something else triggers the vasoplegia response. I know that PAN membranes used in some hemodialyzers and hemoconcentrators need to be rinsed and re-primed with a balanced bicarbonate solution to reduce the risk of bradykinin production. Maybe this mysterious vasoplegia is something similar, but it only occurs in a few select patients.

The AmSECT Safety Committee

Contributor: Gary Grist

FAILURE MODE AND EFFECTS ANALYSIS

FAILURE: Failure to prevent hypotension following phenylephrine, norepinephrine, epinephrine or vasopressin administration during CPB: level III.

EFFECT:

1. Refractory hypotension despite adequate blood flow and treatment with phenylephrine, norepinephrine, epinephrine and vasopressin.

2. Inadequate perfusion of vital organs

3. Temporary or permanent organ damage

4. Failure to wean from CPB.

5. Death

CAUSE:

1. CPB associated vasoplegia of unknown origin.

2. In severe sepsis, excessive formation of NO & c-GMP are associated with profound vasodilatation, hyporeactivity to catecholamines, & myocardial depression. CPB may initiate a systemic inflammatory response syndrome (SIRS) similar to severe sepsis. CPB SIRS causes endothelial production and release of NO & c-GMP, causing profound hypotension; essentially an anaphylactic response to CPB.

3. Anaphylaxis to antibiotics.

4. Transfusion reaction.

5. Bradykinin is the mediator of hypotensive symptoms in hereditary angioedema (HAE) patients.

6. Persistent LSVC

7. Poorly protected hypertrophic heart ( see section on hypertrophic heart)

8. Intraop MI

9. Alpha gal allergy from tick bite

10. Lidocaine overdose or acute toxicity.

11. Mastocytosis: degranulation of mast cells causing SEVERE anaphylaxis. Stimulated by opiate derivatives, NSAIDs, alcohol and hypothermia.

12. Protamine reaction

13. Histamine reaction

14. Unknown drug allergy or reaction

PRE-EMPTIVE MANAGEMENT:

1. Precaution: Methylene blue (MB) can be used to treat vasoplegia, but it may be contraindicated in patients taking selective serotonin reuptake inhibitors (SSRIs).

2. Heart failure patients and chronically ill patients may take SSRIs for depression.

3. MB may induce serotonin syndrome as a result of its effect on monoamine oxidase activity.

4. Symptoms of serotonin syndrome:

a. Agitation

b. Confusion

c. Tachycardia

d. Hypertension

e. Pupil dilation

f. Muscular spasms or rigidity

g. Diaphoresis

h. Diarrhea

5. SSRIs:

a. Citalopram (Celexa)

b. Escitalopram (Lexapro)

c. Fluoxetine (Prozac)

d. Fluvoxamine (Luvox)

e. Paroxetine (Paxil, Pexeva)

f. Sertraline (Zoloft)

g. Vilazodone (Viibryd)

MANAGEMENT:

1. CPB initiation & cardioplegia delivery can cause a precipitous & refractory drop in the SVR of patients in septic shock.

2. Boluses of α-1 agonists or vasopressin usually reverse this drop in SVR. But, in some cases, this may not normalize SVR.

3. MB, a NO & c-GMP inhibitor, can reverse severe vasodilatory shock. MB inhibits both constitutive & inducible nitric oxide synthase (c-NOS & i-NOS). The additional effect of MB on soluble guanylyl cyclase adds to the inhibition of the NO ⁄ c-GMP pathway.

4. Adult Dosage: 2 mg/kg over 15-20 min

5. Pediatric Dosage: 1 mg/kg during a 1-hour period

6. Epinephrine and Benadryl if antibiotic anaphylaxis is suspected.

7. Consider steroids if inflammatory response is suspected.

8. Consider high-dose intravenous hydroxocobalamin (Vit B12) as an alternative to MB especially in patients taking SSRIs. Vitamin B12 treats vasoplegia by the binding of nitric oxide (NO) and directly inhibiting NO synthase and guanylate cyclase. (Roderique JD et al, 2014).

9. High flow ventricular support may be necessary to wean from CPB or utilized in the immediate postop period.

PRECAUTIONS:

1. MB skin staining & discoloration is known to interfere with pulse & cerebral oximetry.

2. MB blood discoloration is known to interfere with near IR spectroscopy used to measure vSAT in the ECC.

3. MB is contraindicated during pregnancy.

4. MB has the potential to cause hemolytic anemia & hyperbilirubinemia in the newborn.

5. Other safety concerns include oximeter interference, pulmonary hypertension, neurotoxicity, arrhythmias, and potentially altered coronary, mesenteric, and renal perfusion.

RISK PRIORITY NUMBER (RPN):

A. Severity (Harmfulness) Rating Scale: how detrimental can the failure be:

1) Slight, 2) Low, 3) Moderate, 4) High, 5) Critical

(I would give this failure a critical RPN, 5.)

B. Occurrence Rating Scale: how frequently does the failure occur:

1) Remote, 2) Low, 3) Moderate, 4) Frequent, 5) Very High

(The occurrence is low, so the RPN would be a 2.)

C. Detection Rating Scale: how easily the potential failure can be detected before it occurs:

1) Very High, 2) High, 3) Moderate, 4) Low, 5) Uncertain

(The Detectability RPN equals 3. Level III is more difficult to detect because hypotension Levels I and II must first be eliminated as the cause.)

D. Patient Frequency Scale:

1) Only a small number of patients would be susceptible to this failure, 2) Many patients but not all would be susceptible to this failure, 3) All patients would be susceptible to this failure.

(All patients are at risk. So the Patient Frequency RPN should be a 3.)

Multiply A\*B\*C\*D = RPN. The higher the RPN the more dangerous the Failure Mode.

The lowest risk would be 1\*1\*1\*1\* = 1. The highest risk would be 5\*5\*5\*3 = 375. RPNs allow the perfusionist to prioritize the risk. Resources should be used to reduce the RPNs of higher risk failures first, if possible.

(The total RPN for this failure is 5\*2\*3\*3 = 90. )